

REPLACEMENT SHEET

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SUGAR-CONTAINING AMPHIPHILIC OLIGOMERS

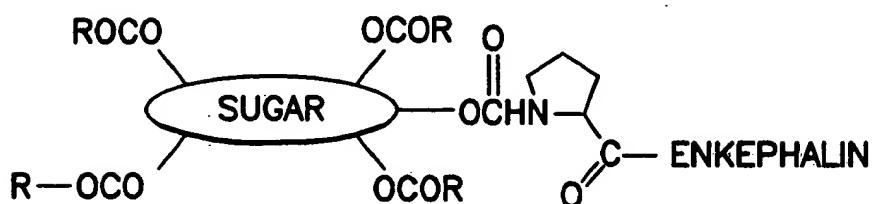


FIG.1A

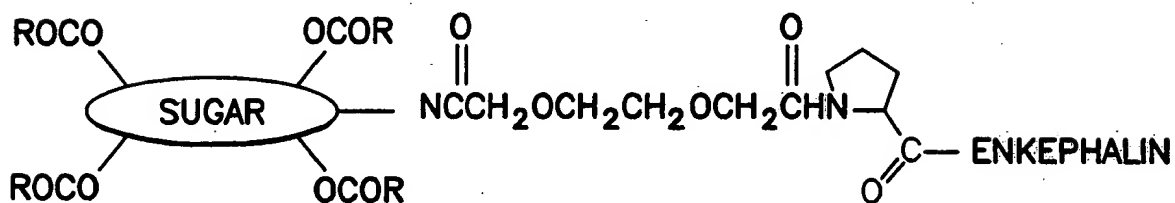


FIG.1B

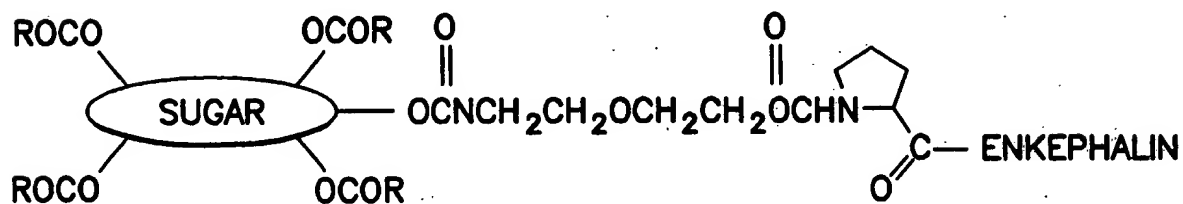


FIG 1C



REPLACEMENT SHEET

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STABILITY OF ENKEPHALIN AND CETYL-PEG₂-ENKEPHALIN
IN RAT BRAIN HOMOGENATE

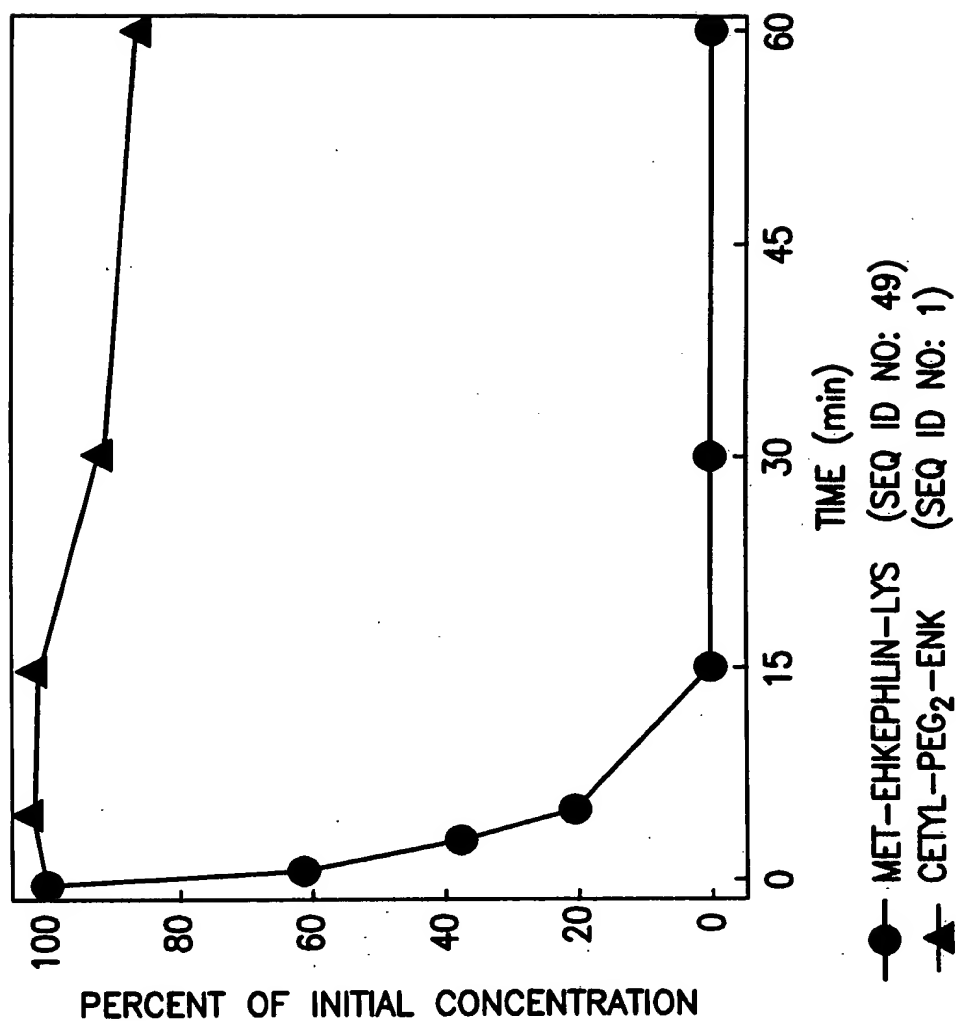
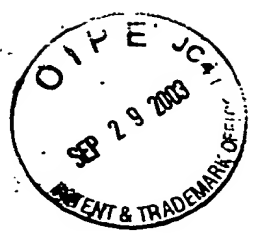


FIG.2



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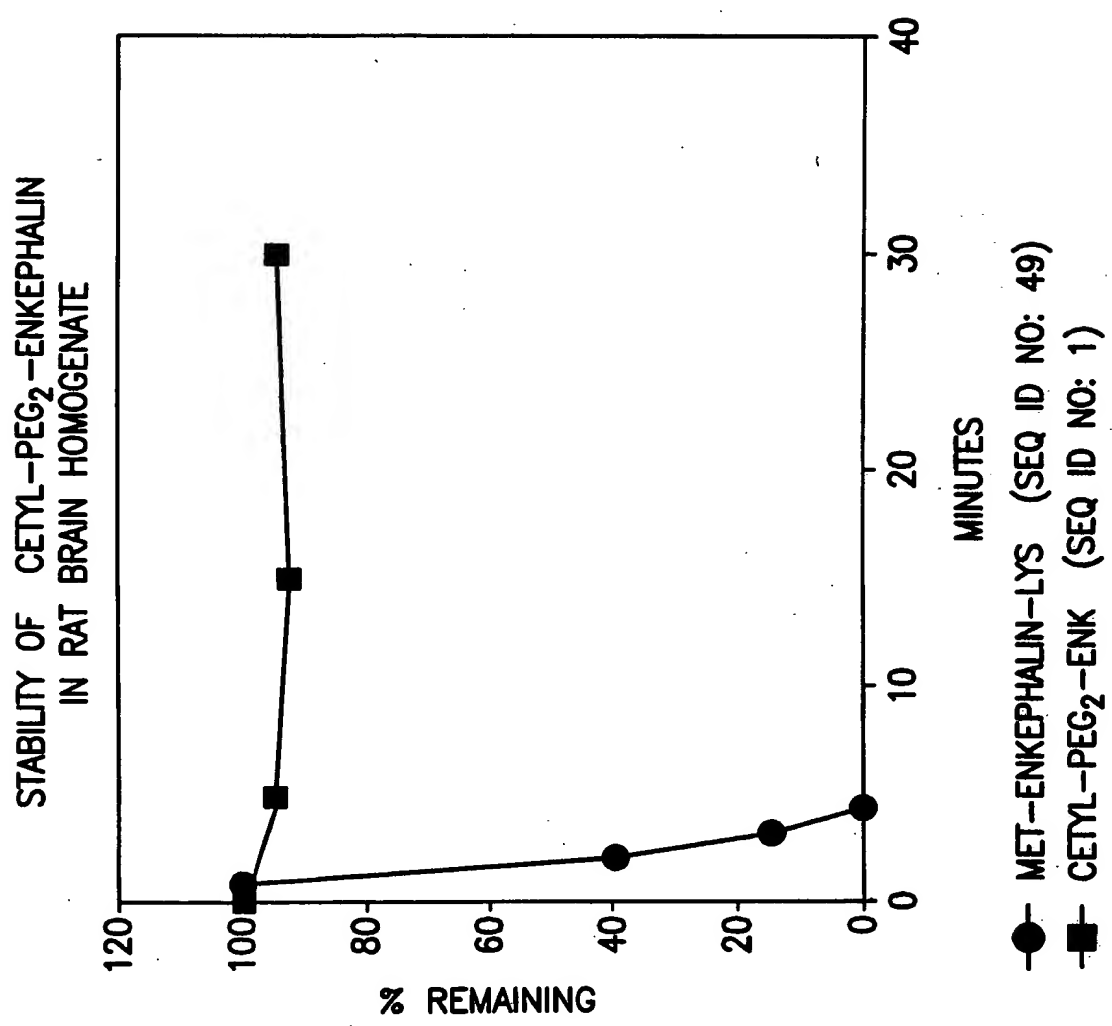


FIG.3



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STABILITY OF PALMITATE-PEG₃-ENKEPHALIN
IN RAT BRAIN HOMOGENATE

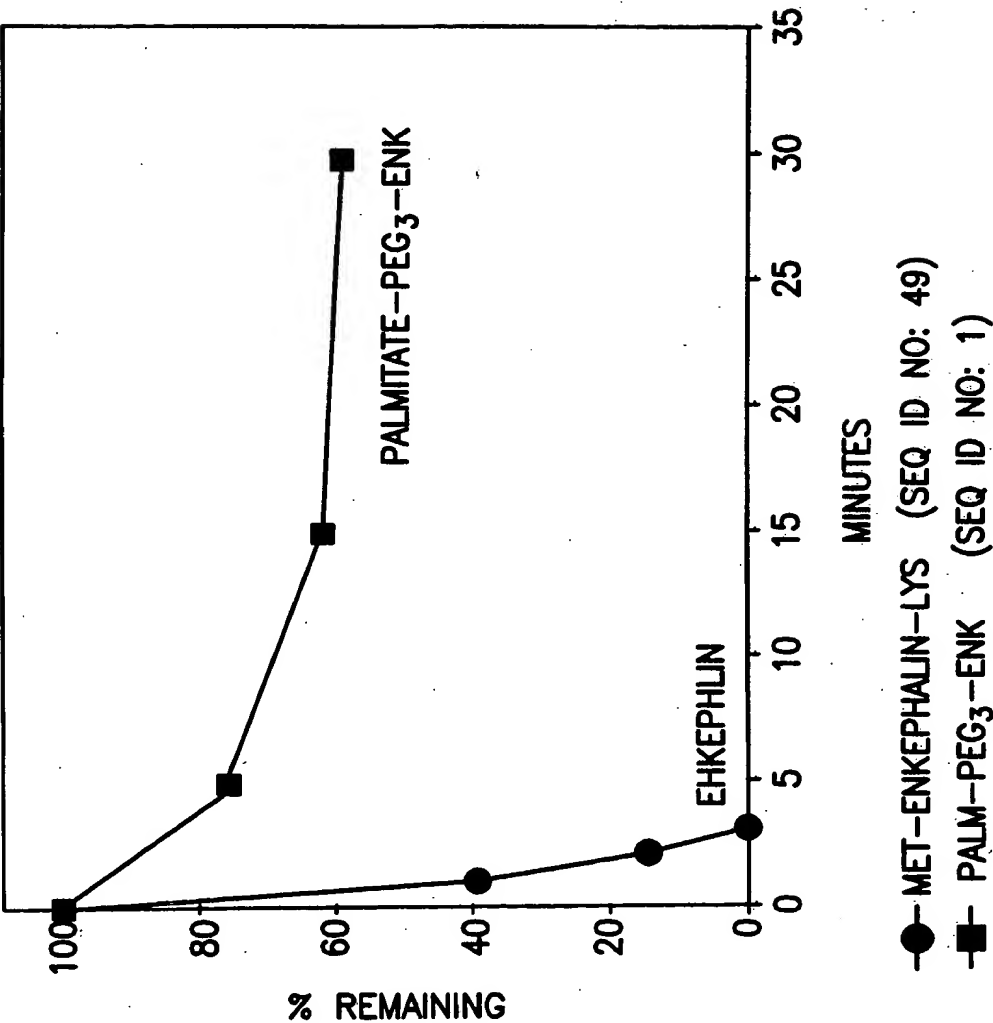


FIG.4



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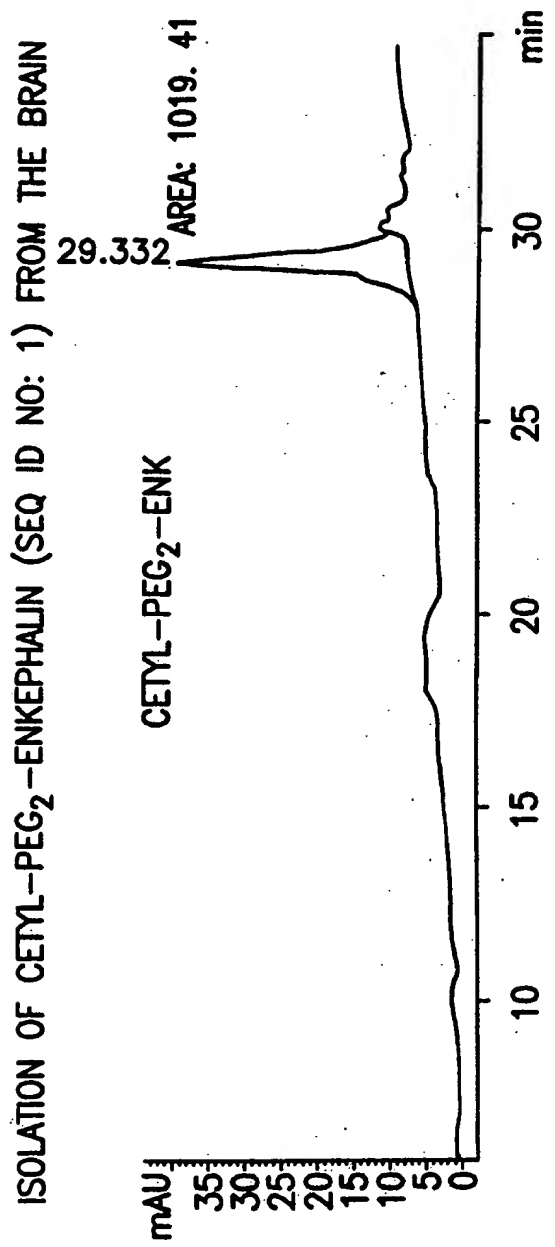


FIG.5A

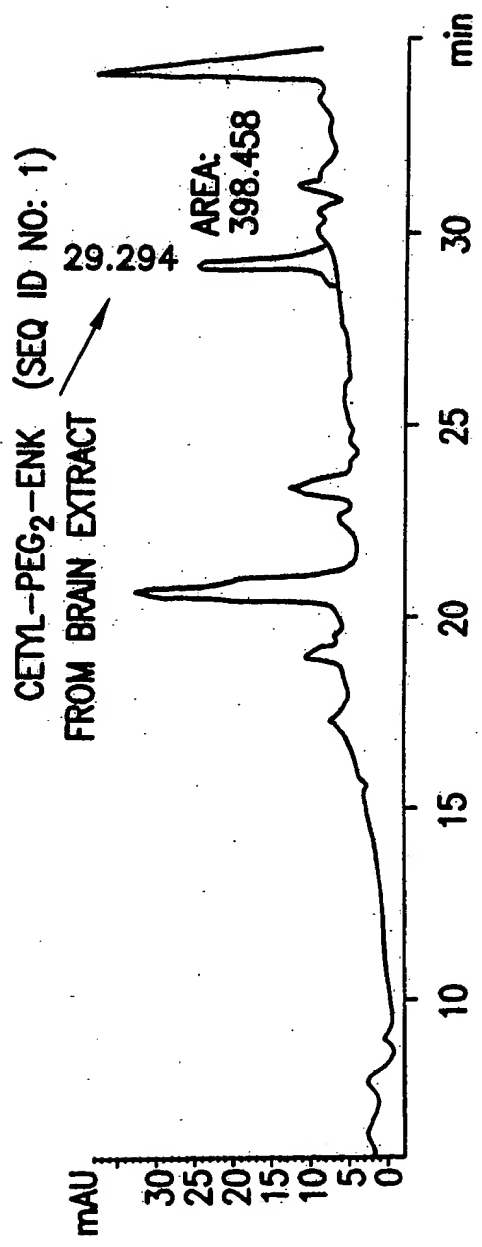
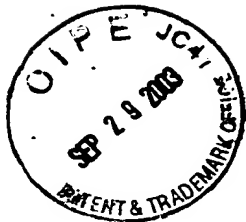


FIG.5B



REPLACEMENT SHEET

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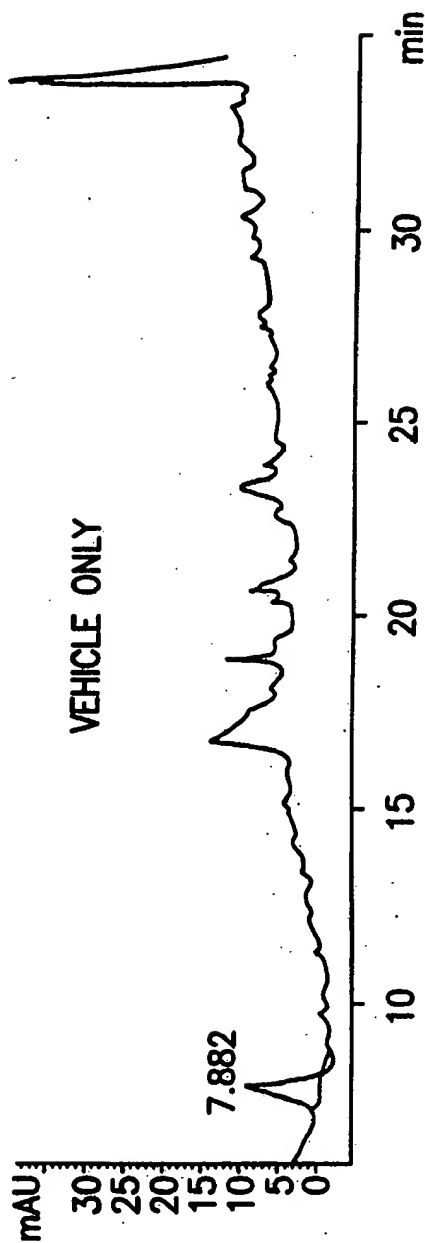


FIG. 5C

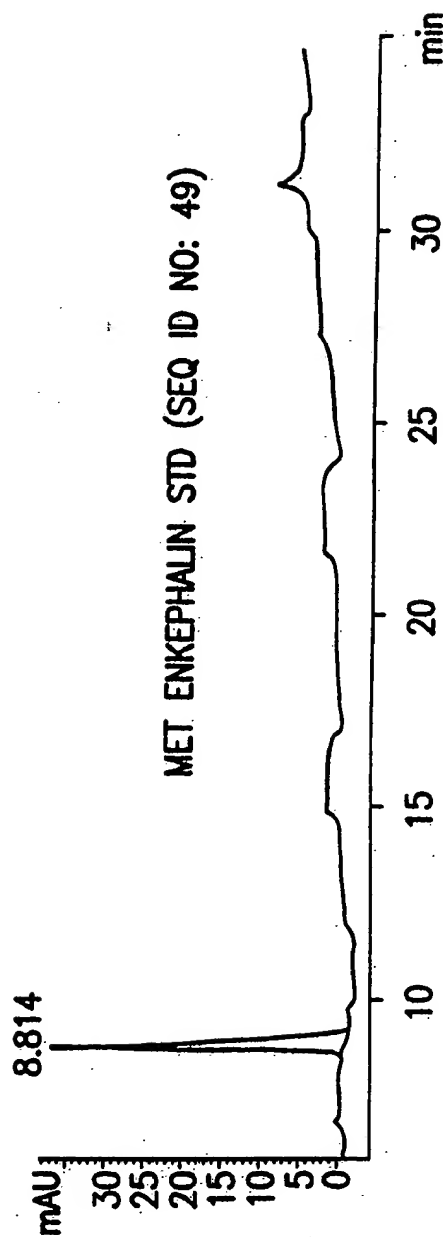
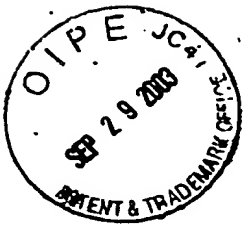


FIG. 5D



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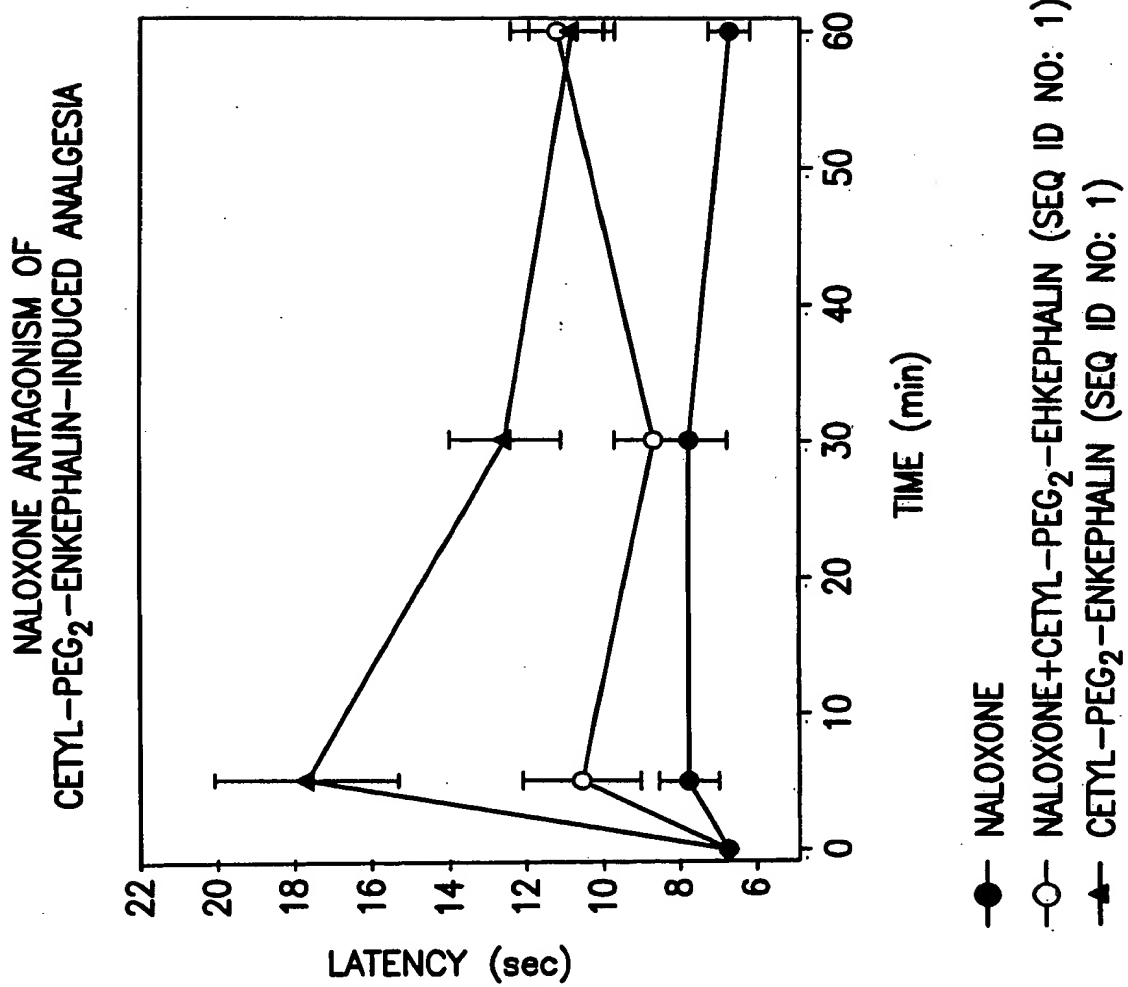


FIG 6

ANALGESIC EFFECT OF A 5 mg/kg IV DOSE OF CETYL-PEG₂-ENKEPHALIN (SEQ ID NO: 1)
MONOCONJUGATE IN THE RAT HOT-PLATE ASSAY

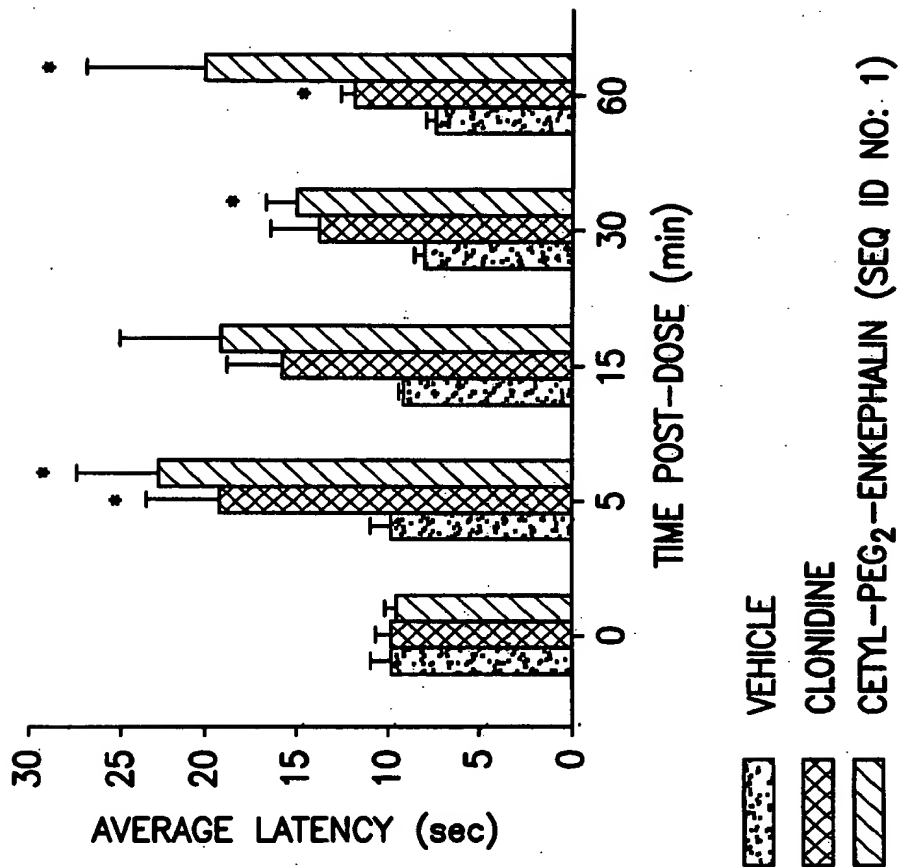
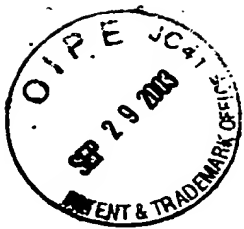


FIG 7

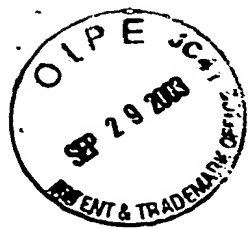




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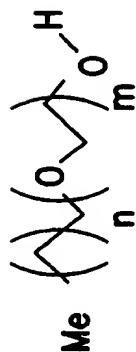
COMPARISON OF μ -RECEPTOR BINDING AFFINITY OF ENKEPHALIN CONJUGATES		
DRUG OR CONJUGATE	DETAILED STRUCTURE	% SPECIFIC BINDING
NALOXONE	NALOXONE	100
ENKEPHALIN	MET-ENKEPHALIN-LYS (SEQ ID NO: 49)	67
CETYL-ENK	CETYL-PEG ₂ -ENK (SEQ ID NO: 1)	100
CHOL-ENK	CHOLESTEROL-PEG ₃ -ENK (SEQ ID NO: 1)	95
DHA-ENK	DHA-PEG ₂ -ENK (SEQ ID NO: 1)	63
PALM-ENK	PALMITATE-PEG ₃ -ENK (SEQ ID NO: 1)	76
CETYL-TEG-ENK	CETYL-PEG ₃ -ENK (SEQ ID NO: 1)	100

FIG.8



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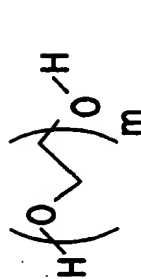
SYNTHESIS OF OLIGOMER



AMPHIPHILIC POLYMER



$\text{Me}-(\text{CH}_2)_n\text{Br}$
(BROMO ALKYL DERIVATIVE)
 $m=15, 17$ etc.



POLYETHYLENE GLYCOL
 $m=0, 1, 2, 3$
(AVERAGE)

"FREE END"

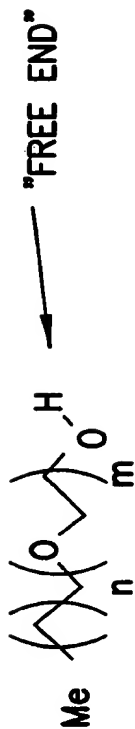


AMPHIPHILIC POLYMER

FIG.9

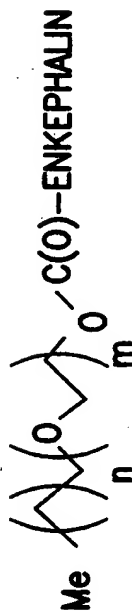
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ATTACHMENT OF OLIGOMER TO ENKEPHALIN



ACTIVATION

ENKEPHALIN



OLIGOMER-ENKEPHALIN-CONJUGATE

EXAMPLE $m=14$ AND $n=2$ CETYL-PEG₂-ENKEPHALIN

FIG 10